Inflammatory Bowel Disease
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PATHOPHYSIOLOGY

CROHN DISEASE

Pathology
Crohn disease is characterized by segmental, transmural, granulomatous inflammatory changes that can occur anywhere along the gastrointestinal tract from the mouth to the perianal area. Disease of the terminal ileum is present in 80% of patients with Crohn disease, and 50% of patients have ileocolitis. Approximately 33% and 20% of patients demonstrate only ileal and colonic involvement, respectively. The finding of skip lesions between areas of normal bowel and cobblestoning of the intestinal mucosa is classic for Crohn disease. Chronic inflammation commonly leads to bowel stenosis.

Epidemiology
The yearly incidence of Crohn disease is between 3 and 14 cases per 100,000 people in North America, with a disease prevalence of 26 to 201 cases per 100,000. The incidence rate of Crohn disease has risen steadily, with the highest incidence found in North America and Northern Europe. Crohn disease is more common in Caucasian and Latino people in the United States than in African Americans, Native Americans, and Asian Americans. Women have a 20% to 30% higher incidence than men do.

The cold chain hypothesis suggests that the rise in incidence of Crohn disease has been associated with the development of home refrigeration techniques. Bacteria that thrive in refrigerated foods, such as Yersinia and Listeria, are thought to play a role in stimulation of the immune and inflammatory responses that ultimately lead to Crohn disease. Exacerbations of Crohn disease may be worsened during periods of higher physiologic or mental stress. Other environmental factors such as cigarette smoking, use of nonsteroidal anti-inflammatory drugs (NSAIDs), increased refined sugar intake, increased dietary fat, and decreased fiber intake have been linked to the development of Crohn disease.

Patients receiving immunosuppressant therapy have increased susceptibility to opportunistic infections.

PERSPECTIVE

Approximately 1 million people in the United States suffer from inflammatory bowel disease (IBD). The two major forms of IBD are Crohn disease and ulcerative colitis (UC). The incidence of both disease processes is similar, although Crohn disease appears to be increasing. Each disease may relapse and remit, with exacerbations that often require emergency care and hospitalization.

IBD has a familial predilection, with an absolute risk of 7% among first-degree relatives. Up to a fifth of patients with IBD have an affected first-degree family member. Ashkenazi Jewish populations continue to have the highest documented incidence per capita of any group in the world. Hispanic and African American populations have a lower incidence of IBD than the Caucasian population does.

The age at onset of IBD is bimodal. The greatest numbers of new cases are diagnosed in patients 15 to 35 years of age. Classically, a second peak is observed during the sixth decade of life. Advances in diagnostic testing have probably contributed to an overall rise in the number of new cases of IBD, as well as to the identification of the disease in younger patients.

KEY POINTS

- Acute exacerbations of inflammatory bowel disease are characterized by abdominal pain, nausea, vomiting, diarrhea, and gastrointestinal bleeding.
- Life-threatening complications include bowel obstruction, hemorrhagic shock, toxic megacolon, malabsorption, abscess formation, and sepsis.
- Treatment with analgesics, intravenous hydration, antiemetics, and electrolyte replacement should occur in parallel with appropriate diagnostic imaging and laboratory studies.
- Antibiotics, steroids, and immunosuppressant therapies can be used in conjunction with specialty consultation.
- Hypersensitivity reactions may result from long-term immunomodulator and antiinflammatory therapies.
- Patients receiving immunosuppressant therapy have increased susceptibility to opportunistic infections.
CHAPTER 36  INFLAMMATORY BOWEL DISEASE

Clinical Presentation
Patients with Crohn disease typically have abdominal pain, fever, diarrhea, and weight loss. Because Crohn disease involves the entire gastrointestinal tract, patients may suffer from oral ulcers, odynophagia, dysphagia, and symptoms of gastric outlet obstruction. Sinus tracts may develop and lead to common complications such as abscesses and fistula formation. Patients with Crohn disease can also have gastrointestinal bleeding, though to a lesser extent than patients with UC. Other complications include bowel obstruction, fissures, malignancy, malabsorption, malnutrition, and hypocalcemia.

Crohn disease is associated with an increased risk for demyelinating diseases, as well as a higher incidence of inflammatory processes such as asthma, arthritis, bronchitis, psoriasis, and pericarditis.16,17 Approximately 20% of patients with Crohn disease experience one or more of the following extraintestinal manifestations of disease during their lifetimes: ankylosing spondylitis, uveitis, episcleritis, hepatitis, cholelithiasis, pancreatitis, primary sclerosing cholangitis, cholangiocarcinoma, nephrolithiasis, and erythema nodosum (Fig. 36.1; Box 36.1).

ULCERATIVE COLITIS
Pathology
UC is a recurring inflammatory disease confined to the mucosal layer of the colon and rectum only. Areas of inflammation are continuous, not segmental; patients commonly experience ascending disease from the rectum to the colon. Isolated rectal involvement is present in a minority of patients.

Epidemiology
The yearly incidence of UC is relatively constant—in the United States it is 8 per 100,000 people, with a disease prevalence of 246 cases per 100,000 people.18,19 The etiology of this disease is unknown, although certain risk factors have been identified. UC is most commonly found in North American and Northern European Caucasian populations. In addition, similar to Crohn disease, development of UC has been linked to the use of NSAIDs, increased refined sugar intake, increased dietary fat, and decreased fiber intake.9,11 However, cigarette smoking appears to lessen the risk for development of UC.20

Clinical Presentation
Although UC has variable findings, bloody, purulent, and mucoid diarrhea is considered to be the classic manifestation. Fever, weight loss, dehydration, anemia, and hypoalbuminemia are common. Patients may be categorized as having mild disease (60%), moderate disease (25%), or severe disease (15%). Severe disease is defined as six or more bowel movements per day.

Significant lower gastrointestinal bleeding is the most common complication, with 3% of patients with UC having massive hemorrhage. Patients may also have toxic megacolon as a complication of fulminant colitis. Toxic megacolon causes a loss of colonic muscular tone that results in luminal diameters larger than 6 cm—pathologic changes that increase the risk for perforation and mortality. Long-term complications of UC include bowel strictures and the development of colon cancer.

Patients with UC may have extraintestinal complications such as concurrent arthritis, uveitis, erythema nodosum, pyoderma gangrenosum, and progressive liver disease (Fig. 36.2; Table 36.1).

Diagnosis Testing
Imaging Modalities
Most cases of IBD diagnosed in the emergency department (ED) are found via computed tomography (CT) of the abdomen in patients with severe, unexplained abdominal pain. A presumptive diagnosis of IBD can be based on typical CT findings coupled with the appropriate signs and symptoms. CT enterography has been shown to have 100% sensitivity and 95% specificity for detection of small bowel lesions associated with Crohn disease.21 CT enterography is superior to

Box 36.1 Differential Diagnosis: Colitis

Inflammatory bowel disease:
- Crohn disease
- Ulcerative colitis
- Indeterminate colitis

Infectious colitis:
- Shigella
- Amoeba
- Giardia
- Escherichia coli O157:H7
- Yersinia
- Campylobacter
- Entamoeba histolytica
- Viral infections
- Mycotic infections

Pseudomembranous colitis (Clostridium difficile):
- Diverticulitis
- Sarcoidosis
- Tuberculosis
- Proctitis (including sexually transmitted causes):
- Collagenous colitis
- Irritable bowel syndrome
- Food intolerance

Fig. 36.1 Computed tomography scan showing terminal ileitis (arrow) in a patient with Crohn disease.
standard CT of the abdomen and pelvis in patients with a high pretest probability of Crohn disease (i.e., first-degree family members of patients with IBD). Confirmation of the diagnosis is made by histologic examination of tissue biopsy specimens obtained via inpatient endoscopy or surgery.

Patients seen in the ED with an exacerbation of known IBD do not always require CT. Plain films are generally sufficient to exclude complications such as bowel obstruction and rare perforations. CT should be used to identify abscesses or other intraabdominal disease in patients with peritoneal findings or sepsis.

Other imaging modalities are best used outside the ED. Barium and air-contrast radiographic studies frequently demonstrate classic radiographic evidence of IBD; they are useful tests for obese patients who exceed the weight limit for standard CT scanners. Upper and lower endoscopy allows direct visualization and biopsy of suspected lesions. Technology that enables patients to swallow endoscopic cameras as capsules represents a promising, minimally invasive method to visualize the bowel mucosa.

LABORATORY TESTS

Laboratory studies have limited value in the ED evaluation of IBD. Most tests serve to exclude complications or alternative diagnoses. A complete blood count can provide a baseline hemoglobin level. Leukocytosis is a nonspecific finding in patients with chronic IBD; marked elevations in the white blood cell count may correlate with new abscess formation, toxic megacolon, sepsis, or corticosteroid therapy. A serum chemistry panel is needed to exclude hypokalemia, hypocalcemia, and electrolyte imbalances in patients with severe vomiting and diarrhea. Hypoalbuminemia is often detected with liver function tests. The erythrocyte sedimentation rate and C-reactive protein levels add little value for guiding ED therapy.

Serologic markers may be used to differentiate Crohn disease from UC. The presence of p-ANCA (perinuclease-staining antineutrophil cytoplasmic antibodies) is sensitive and predictive of UC, whereas detection of ASCA (anti—Saccharomyces cerevisiae antibodies) markers probably predicts Crohn disease. These serologic tests are not indicated for use in the ED.

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<thead>
<tr>
<th>Table 36.1 Features of Crohn Disease and Ulcerative Colitis</th>
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<tbody>
<tr>
<td><strong>FINDING</strong></td>
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<td>Location</td>
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<td>Rectal</td>
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<td>Extracolonic</td>
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<td>Ileal</td>
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<td>Signs and Symptoms</td>
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<td>Abdominal pain</td>
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<td>Hematochezia</td>
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<td>Weight loss</td>
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<td>Perianal disease</td>
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<td>Pathologic Findings</td>
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<td>Continuity</td>
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<td>Inflammation</td>
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<td>Oral ulcers</td>
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<td>Perinuclease-staining antineutrophil cytoplasmic antibody (p-ANCA) positivity</td>
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<td>Anti–Saccharomyces cerevisiae antibody (ASCA) positivity</td>
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TREATMENT

GENERAL MANAGEMENT

Exacerbations of IBD are often marked by significant pain, fever, diarrhea, gastrointestinal bleeding, anorexia, and dehydration; severity is most pronounced in patients with chronic disease who seek treatment in the ED because of exacerbations. Management of symptoms should be done in parallel with diagnostic testing. Analgesics, antiemetics, and intravenous hydration should be administered on arrival of the
Inflammatory Bowel Disease

Oral, enema, and suppository preparations of sulfasalazine are available. Oral steroids improve mild to moderate IBD symptoms within days to weeks and are used in patients who do not improve with 5-ASA agents. Prednisone, 40 mg/day, is an acceptable starting dose; equivalent parenteral administration should be reserved for severe disease or for patients who cannot tolerate oral medications. Long-term corticosteroid therapy at a low maintenance dose is often required. Patients with small bowel obstruction secondary to terminal ileitis may have a response to early treatment with steroids, thereby reducing the need for surgical intervention (Fig. 36.5).

Patients with Crohn disease can benefit from maintenance therapy with azathioprine or its active metabolite 6-mercaptopurine (6-MP). These immunomodulator drugs inhibit lymphocytic proliferation and subsequent activation of the inflammatory cascades. Their onset of action is 3 to 5 months in most cases. 6-MP is reserved for patients with disease refractory to other medications. Long-term corticosteroid therapy at a low maintenance dose is often required. Patients with small bowel obstruction secondary to terminal ileitis may have a response to early treatment with steroids, thereby reducing the need for surgical intervention (Fig. 36.5).

Sulfasalazine is a first-line oral agent used for the treatment of mild to moderate IBD. Colonic bacteria cleave the drug into 5-aminosalicylic acid (5-ASA) and sulfapyridine. 5-ASA acts directly on intraluminal lesions without systemic absorption. Although its mechanism of action is still unclear, 5-ASA probably inhibits leukocyte chemotaxis, as well as prostaglandin and leukotriene production. Sulfapyridine is a toxic by-product responsible for a variety of dose-related adverse effects (nausea, vomiting, diarrhea, headache, abdominal pain, arthralgias) and hypersensitivity reactions (rash, bone marrow suppression, fever, pancreatitis, liver disease, nephrotoxicity). Sulfasalazine at doses of 4 g or more per day should produce a clinical response within 3 to 4 weeks. Oral, enema, and suppository preparations of sulfasalazine are available.

Oral steroids improve mild to moderate IBD symptoms within days to weeks and are used in patients who do not improve with 5-ASA agents. Prednisone, 40 mg/day, is an acceptable starting dose; equivalent parenteral administration should be reserved for severe disease or for patients who cannot tolerate oral medications. Long-term corticosteroid therapy at a low maintenance dose is often required. Patients with small bowel obstruction secondary to terminal ileitis may have a response to early treatment with steroids, thereby reducing the need for surgical intervention (Fig. 36.5).

In the setting of refractory emesis or bowel obstruction, nasogastric tube decompression may provide substantial relief. Identification and treatment of electrolyte imbalances, concurrent infections, and hemorrhage should precede hospital admission.

Immunomodulator, antiinflammatory, and antibiotic agents should be given in consultation with the patient’s gastroenterologist. Because these medications often require long-term administration and dose adjustments, complex drug regimens are typical. Treatment algorithms for Crohn disease and UC are summarized in Figures 36.3 and 36.4.

**COMMON MEDICATIONS**

**Sulfasalazine**

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<tr>
<th>Condition</th>
<th>Treatment</th>
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<tr>
<td>Colitis or ileocolitis</td>
<td>Oral 5-ASA drug or metronidazole and/or ciprofloxacin, Continued activity → Prednisone,Continued activity or steroid dependence → Immunomodulator,Continued activity → Surgery or infliximab</td>
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| Fistula | TPN or immunomodulator or infliximab, Failure to close → Surgery |

| Abscess | Antibiotics, drainage, and resection |

| Obstruction due to inflammation | IV fluids, nasogastric suction, parenteral steroids, Failure to respond → Surgery |

| Obstruction due to scarring | IV fluids, nasogastric suction, Failure to respond → Surgery |

| Perianal disease | Antibiotics and surgical drainage |

| Disease in remission | Maintenance with oral 5-ASA drugs or immunomodulators |

**Fig. 36.3** Treatment algorithm for Crohn disease. 5-ASA, 5-Aminosalicylic acid; IV, intravenous; TPN, total parenteral nutrition. (From Goldman L, Ausiello D, editors. Cecil’s textbook of medicine. 22nd ed. Philadelphia: Saunders; 2003.)

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**Fig. 36.4** Treatment algorithm for ulcerative colitis. 5-ASA, 5-Aminosalicylic acid. (From Goldman L, Ausiello D, editors. Cecil’s textbook of medicine. 22nd ed. Philadelphia: Saunders; 2003.)
The antibiotics most commonly used are a combination of metronidazole and ciprofloxacin. The utility of these agents for UC has not been proved.

**SURGERY**

Seventy-five percent of patients with Crohn disease require surgery within the first 20 years after diagnosis. Emergency consultation should be obtained for patients with complications of IBD-related surgery or for patients with suspected life-threatening complications, including massive hemorrhage, abscess formation, obstruction, toxic megacolon, and perforation. Intravenous hydration, nasogastric decompression, and broad-spectrum antibiotic therapy should be given in preparation for surgery.

**DISPOSITION**

Hospital admission is required for moderate to severe exacerbations of IBD. Patients with severe dehydration, systemic infection, abscesses, or potentially life-threatening complications such as hemorrhage, toxic megacolon, perforation, and bowel obstruction must be managed as inpatients. Discharge should be reserved for patients with mild disease in whom oral hydration and pain control are easily attained. Changes in medication and disposition should be decided in consultation with a gastroenterologist.

**SUGGESTED READINGS**


**REFERENCES**

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES


